AMENDMENTS TO THE CLAIMS:

This listing of Claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-52 (canceled)

Claim 53 (currently amended):

A process for increasing the loading efficiency of trehalose into platelets comprising:

providing platelets having a first phase transition temperature range and a second phase transition temperature range which is greater than the first phase transition temperature;

disposing the platelets into a trehalose solution ~~for~~ to commence loading trehalose into the platelets by uptaking trehalose from the trehalose solution by fluid phase endocytosis; and

heating the trehalose solution to the second phase transition temperature range to increase the loading efficiency of trehalose into the platelets.

Claim 54 (canceled)

Claim 55 (previously presented):

The process of Claim 53 wherein said platelets are human platelets.

Claim 56 (previously presented):

The process of Claim 53 wherein said second phase transition temperature range is greater than about 25^0 C.

Claim 57 (previously presented):

The process of Claim 55 wherein said second phase transition temperature range is greater than about 25^0 C.

Claim 58 (canceled)

Claim 59 (canceled)

Claim 60 (previously presented)

The process of Claim 56 wherein said second phase transition temperature ranges from a temperature greater than about 25^0 C to a temperature less than about 40^0 C.

Claim 61 (previously presented)

The process of Claim 55 wherein said second phase transition temperature ranges from a temperature greater than about 25^0 C to a temperature less than about 40^0 C.

Claim 62 (previously presented)

The process of Claim 60 wherein said temperature ranges from about 30^0 C to less than about 40^0 C.

Claim 63 (previously presented)

The process of Claim 61 wherein said temperature ranges from about 30^0 C to less than about 40^0 C.

Claims 64-73 (canceled)

74. (new) The process of Claim 53 wherein said increasing the loading efficiency of trehalose into platelets additionally comprises maintaining a concentration of the trehalose in the trehalose solution at less than about 50 mM.

75. (new) The process of Claim 53 wherein said loading with an trehalose includes loading with a loading efficiency ranging from about 45% to about 50 % for the trehalose solution having a trehalose concentration ranging from about 20 mM to about 30 mM.

76. (new) A process for preventing a decrease in a loading efficiency gradient in the loading of an oligosaccharide into the platelets comprising:

providing platelets having a first phase transition temperature range and a second phase transition temperature range which is greater than the first phase transition temperature;

disposing the platelets into an oligosaccharide solution to commence loading an oligosaccharide into the platelets;

heating the oligosaccharide solution to the second phase transition temperature range to increase the loading efficiency of oligosaccharide into the platelets; and

maintaining a positive gradient of loading efficiency to concentration of the oligosaccharide in the oligosaccharide solution for preventing a decrease in a loading efficiency gradient in the loading of the oligosaccharide into the platelets.

77. (new) The process of Claim 76 wherein said loading comprises loading by fluid phase endocytosis.

78. (new) The process of Claim 76 wherein said loading with an oligosaccharide includes loading with a loading efficiency ranging from about 45% to about 50 % for the oligosaccharide solution having an oligosaccharide concentration ranging from about 20 mM to about 30 mM.

79. (new) The process of Claim 78 wherein said loading with an oligosaccharide includes loading with a loading efficiency ranging from about 45% to about 50% for the oligosaccharide solution having an oligosaccharide concentration ranging from about 20 mM to about 30 mM.

80. (new) The process of Claim 76 wherein said oligosaccharide comprises trehalose.

81. (new) The process of Claim 79 wherein said oligosaccharide comprises trehalose.

82. (new) The process of Claim 76 wherein said preventing a decrease in a loading efficiency gradient in the loading of the oligosaccharide into the platelets additionally comprises maintaining a concentration of the oligosaccharide in the oligosaccharide solution below about 50 mM.

83. (new) The process of Claim 77 wherein said preventing a decrease in a loading efficiency gradient in the loading of the oligosaccharide into the platelets additionally comprises maintaining a concentration of the oligosaccharide in the oligosaccharide solution below about 50 mM.

84. (new) The process of Claim 76 wherein said oligosaccharide comprises trehalose.

85. (new) The process of Claim 77 wherein said oligosaccharide comprises trehalose.

86. (new) The process of Claim 76 wherein said platelets comprise human platelets.

87. (new) The process of Claim 76 wherein said second phase transition temperature range is greater than about 25^0 C.

88. (new) The process of Claim 76 wherein said second phase transition temperature range ranges from a temperature greater than about 25^0 C to a temperature less than about 40^0 C.

89. (new) The process of Claim 76 wherein said second phase transition temperature range ranges from 30^0 C to 37^0 C.

90. (new) The process of Claim 76 wherein said second phase transition temperature range is about 37^0 C.

91. (new) A process for preventing a decrease in a loading gradient in the loading of an oligosaccharide into the platelets comprising:

providing platelets having a first phase transition temperature range and a second phase transition temperature

range which is greater than the first phase transition temperature;

disposing the platelets into an oligosaccharide solution to commence loading an oligosaccharide into the platelets;

heating the oligosaccharide solution to the second phase transition temperature range to increase the loading efficiency of oligosaccharide into the platelets; and

maintaining a positive gradient of loading efficiency (%) to concentration (mM) of the oligosaccharide in the oligosaccharide solution for preventing a decrease in a loading gradient in the loading of the oligosaccharide into the platelets.

92. (new) The process of Claim 91 wherein said loading comprises loading by fluid phase endocytosis.

93. (new) The process of Claim 91 wherein said loading with an oligosaccharide includes loading with a loading efficiency ranging from about 45% to about 50 % for the oligosaccharide solution having an oligosaccharide concentration ranging from about 20 mM to about 30 mM.

94. (new) The process of Claim 93 wherein said loading with an oligosaccharide includes loading with a loading efficiency ranging from about 45% to about 50% for the oligosaccharide solution having an oligosaccharide concentration ranging from about 20 mM to about 30 mM.

95. (new) The process of Claim 91 wherein said oligosaccharide comprises trehalose.

96. (new) The process of Claim 94 wherein said oligosaccharide comprises trehalose.

97. (new) The process of Claim 91 wherein said preventing a decrease in a loading gradient in the loading of the oligosaccharide into the platelets additionally comprises maintaining a concentration of the oligosaccharide in the oligosaccharide solution below about 50 mM.

98. (new) The process of Claim 92 wherein said preventing a decrease in a loading gradient in the loading of the oligosaccharide into the platelets additionally comprises maintaining a concentration of the oligosaccharide in the oligosaccharide solution below about 50 mM.

99. (new) The process of Claim 91 wherein said oligosaccharide comprises trehalose.

100. (new) The process of Claim 92 wherein said oligosaccharide comprises trehalose.

101. (new) The process of Claim 91 wherein said platelets comprise human platelets.

102. (new) The process of Claim 91 wherein said second phase transition temperature range is greater than about 25^0 C.

103. (new) The process of Claim 91 wherein said second phase transition temperature range ranges from a temperature greater than about 25^0 C to a temperature less than about 40^0 C.

104. (new) The process of Claim 91 wherein said second phase transition temperature range ranges from 30^0 C to 37^0 C.

105. (new) The process of Claim 91 wherein said second phase transition temperature range is about 37^0 C.

REMARKS/ARGUMENTS

Claims 33-52 and 64-73 have been cancelled without prejudice, as these claims were non-elected in a restriction requirement. Claims 54, 58 and 59 have also been cancelled without prejudice. Claims 53, 55-57, and 60-63 are pending in the application, along with newly added Claims 74-105.

Claim 53 as amended is an independent claim. Newly added Claims 76 and 91 are also independent claims. Claims 55-57 and 60-63, along with newly added Claims 74 and 75, are dependent claims depending on independent Claim 53 as amended. Newly added Claims 77-90 and newly added Claims 92-105 are dependent claims respectively depending on newly added independent Claims 76 and 91. Under "**AMENDMENTS TO THE SPECIFICATION**" above, a section to the "Summary of the Invention" of the specification has been added to incorporate the specific language of newly added independent claims 76 and 91.

The Examiner has objected to Claim 54 as allegedly being an improper dependent claim because of form. Claim 54 has been cancelled without prejudice. Claims 58 and 59 were rejected by the Examiner under 35 U.S.C. Section 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regard as the invention. Claims 56 and 59 have also been cancelled without prejudice.

Claims 56, 57 and 60-63 were rejected under 35 U.S.C. Section 112, first paragraph, as allegedly containing subject matter which is not described in the specification. The Examiner alleges that the following is considered new matter: "...a second phase transition temperature range that is greater than about 25^0 C, grater than about 25^0 C to less than 40^0 C, or from about 30^0 C to less than 40^0 C..." For language

in the specification to support the subject dependent claims, the Examiner is respectfully requested to page 8, lines 10 and 24-29, which partly state as follows: "loading the platelets with a protective oligosaccharide at a temperature above about 25^0 C....." and ".....elevated temperature of from greater than about 25^0 C to less than about 40^0 C, more preferably from about 30^0C to less than about 40^0 C, most preferably about 37^0 C.....trehalose loading efficiency begins a steep slope increase at incubation temperatures above about 25^0 C up to about 40^0 C." Thus, the claimed subject matter of dependent Claims 56, 57 and 60-63 is not new matter.

The Examiner has also rejected Claims 53-57 under 35 U.S.C. Section 103(a) as being unpatentable over Beattie et al., 1998 (WO 98/14058) in view of Diniz-Mendes et al., 1999 (Biotechnology and Bioengineering, Vol. 65, No. 5, p. 572-578). Applicants have amended independent Claim 53 to further patentably define the claimed embodiment of the invention over Beattie et al and Diniz-Mendes et al, either taken singly or in combination.

Claim 53 as amended, along with newly added independent Claims 76 and 91, claim platelets having a second phase transition temperature range. Dependent Claims 56, 57 and 60-63, along with newly added dependent Claims 87-90 and 102-105, claims various temperatures and/or temperature ranges for the second phase transition temperature range. Neither Beattie et al nor Diniz-Mendes et al teach or suggest the claimed second phase transition temperature or temperature ranges in combination with the other claimed matter of Claim 53 as amended. Diniz-Mendes et al teaches "heat shock treatment of yeast cells" at 400 C, not in a second phase transition temperature or temperature range as claimed. Thus, Claim 53

as amended is patentably distinguishable over Beattie et al and/or Diniz-Mendes et al.

Claim 53 as amended, along with newly added dependent Claims 77 and 92, claim loading by fluid phase endocytosis, which is patentably distinguishable over Beattie et al and/or Diniz-Mendes et al. Loading by the claimed fluid phase endocytosis for various embodiments of the present invention includes specific formation of vesicles, requiring the involvement of a membrane-coat protein, such as clathrin. The vesicles formed by fluid phase endocytosis bud or pinch off into the cytoplasm, but subsequently fuse with lysosomes. In fluid phase endocytosis there is no leaking of nutrients (e.g., molecules) into the cytoplasm. Thus, the loading of an oligoshaccaride into platelets by fluid phase endocytosis for various embodiments of the present invention is distinct from any loading as suggested, if suggested at all, by Beattie et al and/or Diniz-Mendes et al. Thus, Claim 53 as amended (along with newly added dependent Claims 77 and 91) is further patentably distinguishable over Beattie et al and Diniz-Mendes et al, either taken singly or in combination.

As previously mentioned, Applicants have added independent Claims 76 and 91, and dependent Claims 77-90 and 92-105, to claim additional embodiments of the present invention. Independent Claim 76 claims *inter alia* maintaining a positive gradient of loading efficiency to concentration of the oligosaccharide in the oligosaccharide solution for preventing a decrease in a loading efficiency gradient in loading of the oligosaccharide into the platelets. Independent Claim 91 claims *inter alia* maintaining a positive gradient of loading efficiency (%) to concentration (mM) of the oligosaccharide in the oligosaccharide solution for preventing a decrease in a loading gradient in loading of the

oligosaccharide into the platelets. These claimed features are not taught or suggested by Beattie et al and Diniz-Mendes et al, either taken singly or in combination.

Support in the specification for newly added claims may be found as follows: (i)page 18, lines 17-24 and Figure 3 for illustrating maintaining a positive gradient of loading efficiency to concentration of the oligosaccharide in the oligosaccharide solution for preventing a decrease in a loading gradient in the loading of the oligosaccharide into the platelets; and an increase in loading efficiency for an oligosaccharide concentration up to about 50 mM (support for Claims 53, 74, 76, 82, 83, 91, 97 and 98); (ii)Figure 4 for illustrating maintaining a positive gradient of loading efficiency to concentration of the oligosaccharide in the oligosaccharide solution for preventing a decrease in a loading gradient in the loading of the oligosaccharide into the platelets; and a loading efficiency ranging from about 45% to about 50% for the oligosaccharide solution having an oligosaccharide concentration ranging from about 20 mM to about 30 mM (support for Claims 53, 74-76, 78-79, 91, 93-94 and 97); and (iii) page 9, lines 1-2 for loading by fluid phase endocytosis (support for Claims 53, 77 and 92).

REQUEST FROM PATENT EXAMINER: Applicants filed the subject patent application under the names of John H. Crowe, Fern Tablin, and Nelly Tsvetkova. The Patent Office sent a filing receipt with the following Applicants listed: Willem R. Wolkers, Ann E. Oliver, Naomi J. Walker, John H. Crowe, Fern Tablin, and Nelly Tsvetkova. Applicants corrected the Filing Receipt (a copy of corrected Filing Receipt attached hereto), reflecting that John H. Crowe, Fern Tablin, and Nelly Tsvetkova should be the only Applicants. Would the Examiner please enter the correct Applicants for the subject patent

application and enter confirmation of this in his next Office Action. Thank you.

Accompanying this Response is an Information Disclosure Statement, including PTO-1449 Form. Copies of all the references listed on the accompanying PTO-1449 Form may be found in copending related patent application having Application No. 09/828,627, filed April 5, 2001. The Examiner for this copending related patent application is Leon B. Lankford Jr.(art unit 1651).

All Claims are now in condition for allowance and an early notice of same is respectfully solicited.

Respectfully Submitted,

Date: September 4, 2003

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